REMARKS

In the Office Action of September 25, 2000, claims 97 and 99 were provisionally rejected under 35 U.S.C. 101 as claiming the same invention as claims 7 and 9 of copending U.S. Application No. 08/937,755. In addition, claims 90, 91, 105 and 106 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1, 3-7 and 9 of copending U.S. Application No. 08/937,755.

Claims 88 and 90 have now been cancelled. Moreover, claims 91, 105 and 106 have now been amended. It is not clear to applicants that the amended claims are now either identical to, or obvious over, the designated claims of the copending application. However, in the event that a terminal disclaimer would obviate the rejection of these claims, applicants would be prepared to submit a terminal disclaimer in order to overcome a rejection based on obviousness-type double patenting, should such a rejection still apply after the present amendment.

Claims 88, 90-91 and 105-106 stand rejected under 35 U.S.C. 112, first paragraph, as containing new matter and as lacking support in the specification. Specifically, the Examiner states that the specification does not provide adequate support for the use of morphogens to restore motor function for either spinal cord injuries or amyotrophic lateral sclerosis. This ground of rejection is respectfully traversed.

The claims have now been amended to delete reference to spinal cord injuries and amyotrophic lateral sclerosis. The amended claims are directed to methods for stimulating the production of an N-CAM or L1 isoform in a neuronal cell by contact with a morphogen, and methods for decreasing neuronal cell death associated with a neuropathy or an injury. Antecedent support for the amendment to claim 91 is found in the body of that claim which states that the morphogen stimulates the production of an N-CAM or L1 isoform by an NG108-15 cell. Antecedent support for the amendments to the remaining claims can be found in the data shown in Figs. 2A, 2B and 3 of the specification, as well as on page 9, lines 9-30; page 13, lines 28-32; page 16, lines 1-31; page 70, line 16 to page 72, line 4; and page 76, line 1 to page 80, line 5. Entry of the foregoing amendment is deemed appropriate at this time since it is responsive to the issues raised by the Examiner in the final rejection, and it does not raise any new issues or

require any additional search or consideration on the part of the Examiner. No new claims have been added in this amendment, thus facilitating the Examiner's consideration.

Claims 88, 90, 91, 97, 99 and 105-106 also stand rejected under 35 U.S.C. 112, first paragraph, as not being enabled for treating or preserving motor function or restoring motor function. Moreover, the Examiner has stated that the claimed morphogens are not structurally characterized. This ground of rejection is respectfully traversed.

In response, applicants point out that the present claims are not directed to motor function, but rather the production of an N-CAM or L1 isoform in a neuronal cell, and decreasing neuronal cell death associated with a neuropathy or an injury. In addition, the morphogens presently claimed contain sufficient structural characterization to enable one skilled in the art to practice the invention. The BMP-4 morphogen referred to in the Office Action is not within the scope of claims 97, 99, and claims dependent thereon.

The production of N-CAM by a neuronal cell is shown in Example 6 of the specification. Fig. 3 of the specification shows increased neuronal cell aggregation, which is recognized as a model for neuronal cell function to study neurodegenerative diseases, and the effects of injury or trauma. Example 3 of the specification shows that cell death decreased significantly in a dos-dependent manner in the presence of a morphogen. In contrast, in the absence of the morphogen, the cultured primary cells disassociated and underwent cell necrosis. Accordingly, applicants submit that the claims are now in full compliance with all of the requirements of 35 U.S.C. 112, first paragraph.

Claims 90-91 and 105-106 stand further rejected under 35 U.S.C. as being anticipated by WO 95/06656. This ground of rejection is traversed.

The cited reference describes the morphogen dor3 which is stated to have a sequence at least 70% homologous to the C-terminal seven cysteine domain of OP-1. The reference states that this particular morphogen is effective in treating spinal cord injuries and for preserving or restoring motor function.

The amended claims of this application do not include the morphogen dor3, and the present claims are not directed to motor function. Consequently, there is no basis for retaining this rejection.

In view of the foregoing facts and reasons, this application is now believed to overcome the remaining rejections, and to otherwise be in proper condition for allowance. Entry of this amendment is deemed appropriate at this time since it does not raise any new issues, and does not require any additional search or consideration on the part of the Examiner. Accordingly, withdrawal of the rejections, and favorable action on this application is solicited. The Examiner is invited to contact the undersigned at the telephone number listed below if this is believed to facilitate allowance of this application.

Respectfully submitted,

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MARKED-UP CLAIMS

91. (Twice Amended) A method [of preserving motor function in a mammal afflicted with or at risk of amyotrophic lateral sclerosis] for stimulating the production of an N-CAM or L1 isoform in a neuronal cell, comprising [administering the] contacting the neuronal cell with a morphogen comprising a dimeric protein having an amino acid sequence selected from the group consisting of a sequence:

(a) having [at least 70% homology with] the C-terminal seven-cysteine skeleton of human OP-1, residues 38-139 of SEQ ID NO:5;

(b) having [greater then 60%] the amino acid sequence [identity with said] of the C-terminal seven-cysteine skeleton on human OP-1;

(c) defined by Generic Sequence 6, SEQ ID NO:31; and

(d) defined by OPX, SEQ ID NO: 29.

[wherein said morphogen stimulates production of an N-CAM or L1 isoform by an NG108-15 cell *in vitro*.]

97. (Twice Amended) A method for [restoring motor function in a mammal with amyotrophic lateral sclerosis] decreasing neuronal cell death associated with a neuropathy, comprising [administering to the mammal] contacting said neuronal cell with a morphogen selected from the group consisting of human OP-1, mouse OP-1, human OP-2, mouse OP-2, 60A, GDF-1, BMP2A, BMP2B, DPP, Vgl, Vgr-1, BMP3, BMP5, and BMP6, wherein the [administration of the] morphogen [restores motor function in the mammal] stimulates the production of an N-CAM or L1 isoform in said neuronal cell.

99. (Twice Amended) A method for [restoring motor function in a mammal with a spinal cord injury] decreasing neuronal cell death associated with a chemical or physical injury, comprising [administering to the mammal] contacting said neuronal cell with a morphogen selected from the group consisting of human OP-1, mouse OP-1, human OP-2, mouse OP-2,

60A, GDF-1, BMP2A, BMP2B, DPP, Vgl, Vgr-1, BMP3, BMP5, and BMP6, wherein the [administration of the] morphogen [restores motor function in the mammal] stimulates the production of an N-CAM or L1 isoform in said neuronal cell.

105. (Amended) The method of claim 97 [claim 90] or 99, wherein [said spinal cord injury results from a tumor] the morphogen is human OP-1.

106. (Amended) The method of claim 97 [claim 90] or 99, wherein [said spinal cord injury results from a chemical trauma] the morphogen is mouse OP-1.